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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,896	06/27/2006	Richard Anthony Borman	13849-6	1718

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EXAMINER	
BAEK, BONG-SOOK	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,896	BORMAN ET AL.	
	Examiner	Art Unit	
	BONG-SOOK BAEK	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,10,16,17 and 19-28* is/are pending in the application.

4a) Of the above claim(s) *10,16,23 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9, 17, 19-22, and 25-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of claims

The amendment filed on December 22, 2008 is acknowledged. Claims 1-8, 11-15, and 18 have previously been canceled and new claims 22-28 have been added. Claims 10, 16, and 23-24 have been withdrawn and claims 9, 17, 19-22, and 25-28 are under examination in the instant office action.

Applicants' arguments, filed on December 22, 2008, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application. Responses are limited to Applicants' arguments relevant to either reiterated or newly applied rejections.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9, 17, 19-22, and 25-28 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Nials *et al.* (Cardiovascular Drug Reviews, 11(2): 165-179, 1993).

Nials *et al.* teach AH13205 (trans-2-[4-(1-hydroxyhexyl)phenyl]-5-oxocylco pentaneheptanoic acid) and show its relaxant activity on guinea pig isolated trachea and other EP_2 receptor-containing preparations via prostanoid EP_2 receptor (p166, 4th paragraph, figure 1, and table 1). The reference further teaches that AH13205 has smooth muscle relaxant properties and some anti-inflammatory activity and inhibit the release of inflammatory mediators from human lung fragments and human neutrophils (p176, 2nd paragraph). In addition, Nials *et al.* teach that a PGE_2-related compound (EP_2 receptor agonist) such as AH13205, which possesses both bronchodilatory and anti-inflammatory properties, provides a novel and beneficial approach to the treatment of bronchial asthma, which is an inflammatory lung disease.

The reference is silent about individual stereoisomers of AH13205 as claimed in the instant application, however AH13205 in a racemic mixture inherently contains both stereoisomers, (1R,2S)-2-[4-(1-(R)- hydroxyhexyl)phenyl]-5-oxo-cyclopentaneheptanoic acid and (1R,2S)-2-[4-(1-(S)-hydroxyhexyl)phenyl]-5-oxo-cyclopentaneheptanoic acid.

The reference differs from the instant claims insofar as it does not specifically teach the use of substantially purified form of individual stereoisomer of AH13205 as claimed in the instant application.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use a certain stereoisomer of AH13205 for the treatment of inflammatory lung disease such asthma as taught by Nials *et al.* with reasonable expectation of success because of the following reasons: AH13205, which is taught to be effective for treating inflammatory lung disease such asthma by the prior art, inherently contains its corresponding stereoisomers such as (1R,2S)-2-[4-(1-(R)- hydroxyhexyl)phenyl]-5-oxo-cyclopentanecheptanoic acid and (1R,2S)-2-[4-(1-(S)-hydroxyhexyl)phenyl]-5-oxo-cyclopentaneheptanoic acid, thus the effect of AH13205 is considered as a combined effect of its corresponding stereoisomers. Also, a single stereoisomer would have been expected to be similarly useful as the racemic mixture. In absent of some difference in kind between the various isomers, the skilled artisan would have seen each isomer as prima facie obvious (see *In re Adamson and Duffin*, 125 USPQ 233 (CCPA 1960)). The skilled artisan would have expected stereoisomers to be separable and such separated isomers to exhibit physiological effects similar to those of their racemic mixture at varying levels. Possessing a compound known to contain chiral centers places all the resultant isomers in the skilled artisan's possession. Thus, the use of purified form of one or the other stereoisomer of AH13205 for treatment of inflammatory lung disease such asthma would have been prima facie obvious to the skilled artisan at the time the invention was made in the absence of some difference in kind between the various isomers and superior activity of an individual stereoisomer over the racemic mixture.

Regarding the phrase" substantially pure" form of the claimed compound, when claiming a purer form of a known compound, it must be demonstrated that the purified material possesses properties and utilities not possessed by the unpurified material. Ex parte Reed, 135 USPQ 34,36

(POBA 1961), on reconsideration, Ex parte Reed, 135 USPQ 105 (POBA 1961). Therefore, it would be obvious over the known compound disclosed in the prior art.

With respect to at least 80 % of the claimed compound having its corresponding isomer (RSS) or (RSR), the prior art is silent. However, it is well-known that the racemic form of the prior art compound can have an equal percentage of either (RSS) or (RSR). The modification of the percentage of each isomer does not impart patentable weight over the prior art compound since this kind of adjustment is directly related to optimization of the desired isomeric mixture. Therefore, it would have been obvious to the skilled artisan in the art to be motivated to adjust the racemic mixture of the prior art compound into the claimed composition by routine experimentation; this is because the skilled artisan in the art would expect such a manipulation to be successful and feasible with the purview of the skilled artisan in the art.

Response to Applicants' argument:

Applicants argue that Nials does not teach that AH13205 is useful for the treatment of inflammatory lung disease, thus the skilled artisan would not reasonably expect success and would not be motivated to separate the isomers.

However, Nial teaches that AH13205 relaxes smooth muscle form cats and guinea pigs *in vitro* and on inhalation, is a potent bronchodilator in conscious guinea pigs and furthermore it possesses antiinflammatory activity, inhibiting the release of a range of inflammatory mediators from **human** lung mast cells, eosinophils and neutrophils (last paragraph on page 178), which would result in inhibiting inflammation in lung. Although there is some discrepancy in the activity of bronchodilation among the species, when the entirety of the reference is considered,

one skilled in the art would still be motivated to try to use AH13205 for treating inflammatory lung disease since it has a potent anti antiinflammatory activity in human lung cells. In addition, the patient population of the instant claims is not limited to humans. Thus, the skilled artisan would have expected stereoisomers to exhibit physiological effects similar to those of their racemic mixture or at varying levels. In response to Applicants' argument that there was no motivation for one of skill in the art to attempt to separate the isomers, it would be medicinal chemist's desire to purify and isolate the most active stereoisomer from the racemic mixture in order to avoid undesirable activity of additional stereoisomers.

In response to the arguments that "possession of the racemate doses not equal possession of a stereoisomers of the racemate" and "enantiomer is not anticipated or made obvious by racemat", Applicants' unsuccessful attempt of separation of the stereoisomers does not necessarily mean that other skilled artisan would not enable to separate them. Also, stereoisomers of various compounds have been successfully separated by using chiral stationary phases as evidenced by Gubitz (Chromatogrphia, 30: 555-564, 1990) and Demin *et al.* (J Chromatography B, 672:282-289, 1995). Especially, Demin *et al.* showed that the separation of all possible setereoisomers of hepoxillins A_3 and B_3 (prostaglandine derivative), which have similar chiral centers to those of the instant compound. In addition, applicants did not show unexpected properties of the individual stereoisomer over the racemic mixture. In the Forest case, they demonstrated the failure of various scientists to separate the enantiomers and the unexpected properties of (+)-citalopram and showed that it was unexpected that all of the therapeutic benefit of citalopram would reside in the (+)-enantiomer, resulting in escitalopram having twice the potency of racemic citalopram. In the absence of some difference in kind

between the various isomers and superior activity of an individual stereoisomer over the racemic mixture, the use of purified form of one or the other stereoisomer of AH13205 for treatment of inflammatory lung disease would still have been prima facie obvious to the skilled artisan at the time the invention was made.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BONG-SOOK BAEK whose telephone number is 571-270-5863. The examiner can normally be reached 9:00-6:00 Monday-Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brian-Yong S Kwon/
Primary Examiner, Art Unit 1614
Bbs

BONG-SOOK BAEK
Examiner, Art Unit 1614